

REMARKS

Applicants respectfully request entry of the amendment and reconsideration of the rejection of the claims.

Claims 19, 38, 42, 45, 48, 54, 61 and 72 have been amended to further clarify the claimed invention. Claims 42, 45, 48, 54 and 72 have been amended to correct typographical errors and for claim language consistency. Applicants submit the amendment does not introduce any new matter and places the claims in condition for allowance.

Claim Objections

Claims 19, 38, and 59 were objected to as not limited to the elected invention. The Office Action did not provide any rationale for the rejection. Applicants submit the claims as amended are directed to the elected invention. If the Examiner believes the claims as amended are not limited to the elected invention, Applicants respectfully request that the Examiner provide a basis for the objection.

Enablement

Claims 19, 38, and 42-75 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The Office Action alleges claim 38 lacks enablement because specification does not disclose that the claimed method can be used to determine the presence of or predisposition to all types of cancers. Applicants respectfully do not agree. However, without acquiescing to the rejection and solely for the purpose of advancing prosecution, claim 38 has been amended to recite detecting cancer in only certain types of tissue. The amendment is supported by working Examples 3 and 4. Applicants reserve the right to pursue the canceled subject matter in a continuation application.

The Office Action also alleges the tumor marker data provided in the specification does not enable the full scope of the claims. Applicants respectfully do not agree.

The Examiner alleges it is unclear if the nucleic acid levels are enhanced or decreased compared to normal control tissues because of inconsistent expression of the nucleic acid

molecules in the same tissues and concludes it is not clear which samples are statistically significant.

Applicants submit that the Examiner is requiring Applicants to establish enablement to a higher degree of certainty than is required. An enabling disclosure only requires a reasonable correlation to the scope of the claims. As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement is satisfied (*In re Fischer*, 427 F.2d 833, 839 (CCPA 1970)). For a claimed genus, representative examples coupled with a statement applicable to the genus as a whole are ordinarily sufficient to comply with the enablement requirement (MPEP § 2164.02).

The claims have been amended to recite detecting an alteration in expression of the nucleic acid molecules in a tumor cell compared to a normal cell. Table 8 shows expression of the nucleic acid molecules is altered in pancreas, liver, colon, stomach, thyroid, kidney, and bladder cancer cells relative to normal cells from the respective tissues. Table 9 shows expression of the nucleic acid molecules in tumor tissue compared to normal adjacent tissue in the same patient or normal tissue from a different patient. In some instances, expression of the nucleic acid molecules is increased relative to the control (see, for example, colon and liver in Tables 8 and 9). In some instances, expression of the nucleic acid molecules is decreased relative to the control (see, for example, kidney and prostate). Nevertheless, an increase or decrease in expression of the nucleic acid molecules in tumor cells or tumor tissue relative to the control cells or control tissue was indicative of cancer.

Applicants submit the data provide in Tables 8 and 9 provide a reasonable correlation between an alteration in expression of the nucleic acid molecules in the recited cells and tissues and cancer. Contrary to the Examiner's assertion, Tables 8 and 9 provide a control cell or control tissue for each cell type or tissue type. In Table 9, many of the controls are normal adjacent tissue from the same patient.

Citing Barker et al. and Anderson et al., the Examiner alleges that *in vitro* results acquired from tumor cell lines may not correlate with the results obtained from tumor tissue from patients because the cell culturing process alters gene expression and selects subgroups of cells

such that the cultured tumor cells are no longer representative of the diseased tissue. Applicants respectfully do not agree.

If the particular model is recognized in the art as correlating to a specific condition, then the model should be accepted as correlating unless the Examiner has evidence that the model does not correlate. *In re Brana*, 34 USPQ2d, 1436, 1441 (Fed. Cir. 1995); MPEP § 2164.02. A rigorous or an invariable exact correlation is not required. *Cross v. Iizuka*, 244 USPQ, 739, 747 (Fed. Cir. 1985).

Applicants submit that the references cited in the Office Action do not provide sufficient evidence that all tumor cell lines are not representative of the tumor cells *in vivo*. Barker et al. contemplates ovarian tumor cells and only discloses that passage of ovarian tumor cell lines occasionally results in lack of experimental reproducibility. Anderson et al. identified changes in immunological phenotype of glioblastoma cells cultured *in vitro* but the functional significance of the changes was not known. In contrast, Applicants studied the expression of the nucleic acid molecules in several tumor cell lines and tumor tissue from patients. In contrast to Anderson et al., Applicants disclose expression of the nucleic acid molecules in the tumor cell lines (Table 8) correlated with expression of the nucleic acid molecules in tumor tissue (Table 9). For example, expression of the nucleic acid molecules was increased in both liver tumor cells and liver tumor tissue relative to their respective control liver cells and control liver tissue.

Applicants therefore submit the Office Action does not establish that all tumor cell lines are not representative of the tumor cells *in vivo*. Moreover, none of the particular cell types recited in the claims is disclosed in Barker et al. or Anderson et al.

The Office Action alleges claim 59 is not enabled by the specification because the specification does not teach functional characteristics or mechanisms of action of FCTRX. Applicants respectfully do not agree.

Claim 59 further describes a characteristic of the recited inflammation or cancer. The claim does not recite that FCTRX induces the cell proliferation. The claim merely recites that the inflammation or cancer identified by an alteration in expression of FCTRX is a disease or disorder characterized by hyperproliferation and/or loss of control of cell proliferation. Uncontrolled cell proliferation is a characteristic of many of the tumor cells and tumor tissues exemplified in Tables 8 and 9, and working Examples 3 and 4 clearly demonstrate that an

alteration in expression of FCTRX is a useful marker for identifying the cancerous cells and tissues.

The Office Action alleges the specification does not enable methods for determining the presence of inflammation. The Examiner alleges TNF-alpha is a multifunctional cytokine that exerts a myriad of diverse biological functions and that TNF alpha induced expression of the nucleic acids is not tantamount to indicating the presence of inflammation. Applicants respectfully do not agree.

The claims recite methods for detecting inflammation comprising detecting an alteration in expression of the nucleic acids in airway epithelium cells. The specification discloses administering TNF alpha and IL1 beta to the airway epithelium cells. Administering TNF alpha and IL1 beta to airway epithelium cells is an art accepted model of inflammation. See, for example, Cooper et al., 2001, *Am. J. Physiol. Lung Cell Mol. Physiol.*, 280:L841-L852. Airway epithelium cells were known to respond to the inflammatory cytokines TNF alpha and IL1 beta and the coexpression and synergistic effect of TNF alpha and IL1 beta was known to be important for disease pathology in acute and chronic inflammatory conditions (see Cooper et al. at pages L841 and L849). These cytokines are also believed to play an important role in respiratory inflammation observed in chronic bronchitis, chronic obstructive pulmonary disease, and asthma (see Cooper et al. at page L841). Moreover, the Office Action has not provided any evidence that the model does not correlate to inflammation.

Contrary to the Examiner's assertion, Lackman et al. provides further enabling evidence for the pending claims. Lackman et al. discloses that CP-10, also a member of the S100 family, is involved in inflammation and is a chemoattractant for inflammatory cells. In view of the working examples in the specification and Lackman et al., one of skill in the art would have reasonably expected that an alteration in nucleic acid expression of a S100 family member in a model of inflammation would be useful for indicating the presence of inflammation.

The Office Action alleges the specification fails to provide guidance as to what level of expression of a nucleic acid encoding SEQ ID NO:3 or SEQ ID NO:6 would be indicative of a predisposition to cancer or inflammation. Applicants respectfully do not agree. However, without acquiescing to the rejection and solely for the purpose of advancing prosecution, claim

38 as amended is directed to detecting inflammation or cancer. Applicants reserve the right to pursue the canceled subject matter in a continuation application.

The Office Action alleges a nucleic acid molecule encoding a polypeptide having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:6 is not enabled by the specification. Applicants respectfully do not agree. While not acquiescing to the rejection and solely to expedite prosecution, Applicants' claims now refer to a nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:6.

In view of the forgoing, Applicants submit the claims as amended are fully enabled by the specification. Withdrawal of the enablement rejection is respectfully requested.

Written Description

Claims 19, 38, and 42-75 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse this rejection.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. MPEP § 2163(I) (emphasis added). An Applicant may show possession of an invention by disclosure of sufficiently detailed, relevant identifying characteristics (i.e. complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between structure and function, or some combination of such characteristics) that provide evidence that Applicant was in possession of the claimed invention. *Enzo Biochem v. Gen-Probe*, 323 F.3d 956, 964 (Fed. Cir. 2002); MPEP § 2163(II)(3)(A)(a). An actual reduction to practice, however, is not required for written description. *Falkner v. Inglis*, No. 05-1324, slip. op. at 13 (Fed. Cir. May 26, 2006).

The written description requirement must be applied in the context of the particular invention and state of the knowledge. *Capon v. Eschar*, 76 USPQ2d 1078, 1084 (Fed. Cir. 2005). It is unnecessary to spell out every detail of the invention in the specification. Only enough must be included to convince a person of skill in the art that the inventor possessed the

invention. *Falkner v. Inglis*, No. 05-1234, slip. op. at 14 (Fed Cir. May 26, 2006) (citing *LizardTech, Inc. v. Earth Resource Mapping, PTY, Inc.*, 424 F.3d 1336, 1345 Fed. Cir. 2005).

Applying these standards, Applicants submit the specification sufficiently describes the claimed genus of polypeptides for the reasons discussed in the Response filed on November 13, 2006. While not acquiescing to the rejection and solely to expedite prosecution, Applicants' claims now refer to a nucleic acid encoding a polypeptide comprising the amino acid sequence of SEQ ID NO:6.

Interview Request

Applicants request an interview with the Examiner and her supervisor upon receipt of these papers.

Indefiniteness

Claims 19 and 42-50 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Applicants submit claim 19 as amended fully complies with § 112, second paragraph. Withdrawal of the rejection is respectfully requested.

Summary

In view of the above amendments and remarks, Applicants submit the claims are in condition for allowance and respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

Respectfully submitted,

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